U.S. Patent Application No. 10/076,069
Inventor:. JURECIC et al.
Title: "HEPP, A Novel Gene with a Role in
Hematopoietic and Neural Development"
Docket No. 39532-176599
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FIG. 1A

```
   1 CCCCGCGTCGGTCTTCCACCTCACCTTTCGAGCTGGCCGCCGCTTGCTGTGCGCAGTTTC    60
  61 GGGGGACTGGACCTTCCCTGGCTTTTAGCAGCGCCGAGCGCCATGGCGACCCTTTGCTGG   120
 121 GCAGGTGACCGATTCCGGGTGCCCGAAGGAGCTGGCGTGGGTCTGCCTTGCAGCCGCCCG   180
 181 CCTGGACAGGATGTTTGCTAGAGGGCTGAAGAGGAAATATGGTGACCAGGAAGAAGGAGT   240
   1           M  F  A  R  G  L  K  R  K  Y  G  D  Q  E  E  G  V    17
 241 AGAGGGTTTTGGCACTGTCCCTTCCTATAGCCTGCAGCGACAGTCACTCCTGGACATGTC   300
       E  G  F  G  T  V  P  S  Y  S  L  Q  R  Q  S  L  L  D  M  S    37
 301 CCTTGTCAAGCTCCAGCTCTGTCACATGCTAGTGGAGCCCAATCTCTGCCGCTCGGTCCT   360
       L  V  K  L  Q  L  C  H  M  L  V  E  P  N  L  C  R  S  V  L    57
 361 CATCGCCAACACAGTCCGGCAGATCCAGGAGGAAATGAGCCAGGATGGTGTGTGGCATGG   420
       I  A  N  T  V  R  Q  I  Q  E  E  M  S  Q  D  G  V  W  H  G    77
 421 GATGGCACCCCAGAATGTAGATCGGGCACCAGTTGAACGCCTGGTGTCCACAGAGATCCT   480
       M  A  P  Q  N  V  D  R  A  P  V  E  R  L  V  S  T  E  I  L    97
 481 GTGTCGTACAGTGAGGGGAGCTGAGGAAGAGCACCCTGCTCCTGAACTGGAAGATGCTCC   540
       C  R  T  V  R  G  A  E  E  E  H  P  A  P  E  L  E  D  A  P   117
 541 CTTGCAAAACTCGGTTTCCGAGCTCCCCATCGTTGGCTCAGCACCAGGGCAAAGGAACCC   600
       L  Q  N  S  V  S  E  L  P  I  V  G  S  A  P  G  Q  R  N  P   137
 601 TCAGAGCAGCCTCTGGGAGATGGACAGCCCACAAGAAAACAGGGGAAGCTTTCAGAAGTC   660
       Q  S  S  L  W  E  M  D  S  P  Q  E  N  R  G  S  F  Q  K  S   157
 661 ACTGGACCAGATATTTGAGACCCTGGAGAACAAAAACTCCAGTTCAGTGGAGGAACTCTT   720
       L  D  Q  I  F  E  T  L  E  N  K  N  S  S  V  E  E  L  F   177
 721 CTCAGATGTGGACAGCTCCTACTATGACCTGGACACAGTGCTAACAGGAATGATGAGTGG   780
       S  D  V  D  S  S  Y  Y  D  L  D  T  V  L  T  G  M  M  S  G   197
 781 GACCAAGTCCAGTCTCTGCAATGGCCTTGAGGGCTTTGCTGCAGCCACCCCTCCTCCCAG   840
       T  K  S  S  L  C  N  G  L  E  G  F  A  A  A  T  P  P  P  S   217
 841 TTCCACTTGCAAGTCTGACCTGGCTGAGCTGGACCATGTGGTAGAGATTCTGGTGGAGAC   900
       S  T  C  K  S  D  L  A  E  L  D  H  V  V  E  I  L  V  E  T   237
 901 CTGAGAGGCCACCCCAGTGGGCTAAGGGTGAGGCCACCAGTCCCCATGGAGCTCACGTGT   960
       *
 961 GTTGTGACCCAGAGACAGATAAGCACTTGTCCTAAGAGGGGCTCTGGCTCTTGAGCTCAT  1020
1021 TATCCTTTTGTGTGACATTGGACTCACTGTGGAGGATGGTGTGTCACAGCTATGTCTAGT  1080
1081 CTATTTTCAATTAGATAGGTGAACTTTCTAAAATTAAGTTTTATATGTTTTTGGGCAATA  1140
1141 TTTTGTCTTAAGATATATTTTTTAAACTTTTTATACTTTAGATTTTTTTCAGCTATTTTC  1200
1201 TTAAAAGTATATTTTTTCTACAAACATCCTCTGCTGCTACATTAGAAACATTTATAACCT  1260
1261 AAATACGATTGGTGTGTCATTTTAAAGGTTTAAATAGAAAACTTCTTTTGTTACTGAGTC  1320
1321 TCTACACTCCCAAGGCAACTGTAAATGTAGCCGGCCGGGTGTTTACATGAGAGGCTCCAG  1380
1381 TATGGTCTACATTCTAGTAGAGCTTGAAAAGAACCATGCACAGCTCCACTGCCCCCTCAC  1440
1441 TGGGTCTGCTCTGGCGGATCGGAGCTCTCTTCCTAGCCCCGTGTGCAGGATGGCTTTATT  1500
1501 TATGCCTATTTATATGTAAATGCCACTGAAAGCTAAGGTCTTACTCCTGGAAATCCCAAC  1560
1561 ACCAGTTCTTCAGGGACTGCTGTGAGGCAGTGCCTTATGCAGGTCTTGTCCTTGGCCATC  1620
1621 ACTGTCTGGTTCCCAGCCCAGCACATGTGACATGAGGACATGACATGCCCGAACCACCCA  1680
1681 GCACCACATGCTCCATGTCAAGTGTGTACGTGGAGACCACTGGCTCCCAGGCCTGTGCTC  1740
1741 AGAGAGGGTGTGCAGTCCTACGTGTGCTGGGGGGGACGACGGTGACCTGTGCTTGCTTGC  1800
1801 TTTTAAAATGGTGCTTGGACGTTTTAAGGTTAAAAACAATCCGACTCCATATGATTTAGG  1860
1861 GCTCCTCCACCCTGGGGTGGCCCCTATGCTGTCTGCTTGGATCTCAAAGTCTTGGTACTC  1920
1921 GGCACTGTCAGACTCCACCCCATGTATCCTTTTTGTTTCTCTTGTGCTTTTTTTGGACTT  1980
1981 CCCAACCTGAGCCTAAGGTTTTATTTTATATGTGCTTCAATATCAACAATGTAAACCTCA  2040
2041 CTTTATTAAAAGTATCCAGCAAATGGAAAAAAAAAAAAAAA
```

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FIG. 1B

```
   1 GGGAAGCTGGCGGCACAGCCGTGGCGCCTGGCTGAGCAGAGGACCCGGCGGGCGGCCTCG    60
  61 CGGGTCAGGACACAATGTTTGCACGAGGACTGAAGAGGAAATGTGTTGGCCACGAGGAAG   120
   1                M  F  A  R  G  L  K  R  K  C  V  G  H  E  E  D   16
 121 ACGTGGAGGGAGCCCTGGCCGGCTTGAAGACAGTGTCCTCATACAGCCTGCAGCGGCAGT   180
         V  E  G  A  L  A  G  L  K  T  V  S  S  Y  S  L  Q  R  Q  S   36
 181 CGCTCCTGGACATGTCTCTGGTGAAGTTGCAGCTTTGCCACATGCTTGTGGAGCCCAACC   240
       L  L  D  M  S  L  V  K  L  Q  L  C  H  M  L  V  E  P  N  L   56
 241 TGTGCCGCTCAGTCCTCATTGCCAACACGGTCCGGCAGATCCAAGAGGAGATGACGCAGG   300
         C  R  S  V  L  I  A  N  T  V  R  Q  I  Q  E  E  M  T  Q  D   76
 301 ATGGGACGTGGCGCACAGTGGCACCCCAGGCTGCAGAGCGGGCGCCGCTCGACCGCTTGG   360
       G  T  W  R  T  V  A  P  Q  A  A  E  R  A  P  L  D  R  L  V   96
 361 TCTCCACGGAGATCCTGTGCCGTGCAGCGTGGGGGCAAGAGGGGGCACATCCTGCTCCTG   420
       S  T  E  I  L  C  R  A  A  W  G  Q  E  G  A  H  P  A  P  G  116
 421 GCTTGGGGGACGGCCACACACAGGGTCCAGTTTCTGACCTTTGCCCAGTCACCTCAGCAC   480
       L  G  D  G  H  T  Q  G  P  V  S  D  L  C  P  V  T  S  A  Q  136
 481 AGGCACCAAGGCACCTGCAGAGCAGCGCCTGGGAGATGGATGGCCCTCGAGAAAACAGAG   540
       A  P  R  H  L  Q  S  S  A  W  E  M  D  G  P  R  E  N  R  G  156
 541 GAAGCTTTCACAAGTCACTTGATCAGATATTTGAAACGCTGGAGACTAAAAACCCCAGCT   600
       S  F  H  K  S  L  D  Q  I  F  E  T  L  E  T  K  N  P  S  C  176
 601 GCATGGAAGAGCTGTTCTCAGACGTGGACAGCCCCTACTACGACCTGGACACAGTACTGA   660
       M  E  E  L  F  S  D  V  D  S  P  Y  Y  D  L  D  T  V  L  T  196
 661 CAGGCATGATGGGGGGTGCCAGGCCGGGCCCCTGCGAAGGGCTCGAGGGCTTGGCTCCGG   720
       G  M  M  G  G  A  R  P  G  P  C  E  G  L  E  G  L  A  P  A  216
 721 CCACCCCAGGCCCTAGCTCCAGCTGCAAGTCCGACCTGGGCGAGCTGGACCACGTGGTGG   780
       T  P  G  P  S  S  S  C  K  S  D  L  G  E  L  D  H  V  V  E  236
 781 AGATCCTGGTGGAGACCTGAGCAGGAGCCCTGAGTGCTCACAGCCGCCTCTGACGCATTG   840
       I  L  V  E  T  *                                            241
 841 ACACGTGAGCACTGGCTCCCACGGAGGGTGCGCCTGCCGCCAGCGGCCCAGCCTTGCTGC   900
 901 CCTGTCTGCTGATTCTGAGAAATCCCAGAACAGCCCATTACCAGTGGGGCTGCAGCCCTA   960
 961 GGCCCGTCCCACTCACCTCCCCCCTGTGGAGCGCCAGGCAGAGGCTGTTCTGGAAGGCTT  1020
1021 CTTGTCTTCTGACGTCCCCACAGCCCTGGGCCCCTCGTGTCTCTTTGTGTCCCCCACTGT  1080
1081 AGAGGACGGTGAGCCGCAGCTGCATCAACCTCCTTTTACCTTTAGATAGGTGAATTTTTA  1140
1141 CAATTCAGTTTTACATGTTTTGGGCAGTATTTTGTCTTAAGATATATTTTTTAAACTTTT  1200
1201 TATACCTTATCTCTTTAGATTTTTTCAGCTATTTTCTTAAAAGTATATTTTTTCTATAAA  1260
1261 CATCCTTTGCTGCTACATTAGAACTTTTATAGCCTAAACAATTGCAGTTGGTGTGTTTCA  1320
1321 TTTTTTTAAGGTTTAAATAAGGGTTTTTTGTTTTGTTTTGTTTTTTGCAGTGAGCATCAC  1380
1381 TACAGTCTCAGTCAACAGTGTGAATGTATCATGTTTTACTTTAAATGTGTGTGTGATACT  1440
1441 TCTTCATTATGTCCTGCGCTGCAGTGAGACCTGGGTGAAAATCAGGAGCCGCACACAGCC  1500
1501 ACATCTTCCTAGACCTAAGAGTAAATTATGGAGGATTTTATTTATGTCTATTTATATGTA  1560
1561 AATGTCATTGAAGACAAAGGTCAAATATTTGTCTGTTTGTAGATCACAGGCACCAGTTGG  1620
1621 TCTTCAGGGACCTCATAGCCCCTCGGTGGTGCCTTCTCAAGGCAGTGTTCCTGGAGGCTC  1680
1681 CCATCAGGGTCAGCCCATGCACCTGCCCTGGGTGAGGAAGTAGCATTGCTGCTGGATGAG  1740
1741 AAACGCCTGCGCTGCTCTGTTAGACTGGTGCTGAAACAAAAGGTTAAGGCTAGGTTGAAG  1800
1801 TCTAGAATGAAAGAAATCTGAATCCATGTCATTCATAACCCCTTGATCTGTAGTGTCATG  1860
1861 GGTGCTGCCGCAGGCAGGGAGTGAGCTGGGGGTGCCTGCAGCCTTCCACTCCTGCCCCGC  1920
1921 CTCACCCCACATGCTCCCTGTTTCTCATGCTTTCTCTAACTTCCTCACCCCTTAACCAAA  1980
1981 AAGGTGTGTTTTCTTTTGTGCATATAGCCATTCTTAAATATCAGTGATGTAAACCTCACT  2040
2041 TTATTAAAAAATTATCCAGCAAAAAAAAAAAAAAAAAAAAAAA
```

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FIG. 2

Mouse *Hepp*	1	MFARGLKRKYG----DQEEGVEGFGTVPSYSLQRQSLLDMSLVKLQLCHMLVEPNLCRSV
Human *HEPP*	1	MFARGLKRKCVGHEEDVEGALAGLKTVSSYSLQRQSLLDMSLVKLQLCHMLVEPNLCRSV
Mouse *Hepp*	57	LIANTVRQIQEEMSQDGVWHGMAPQNVDRAPVERLVSTEILCRTVRGAEEEHPAPELEDA
Human *HEPP*	61	LIANTVRQIQEEMTQDGTWRTVAPQAAAERAPLDRLVSTEILCRAAWGQEGAHPAPGLGDG
Mouse *Hepp*	117	PLQNSVSEIPIVGSAPGQRNPQSSLWEMDSPQENRGSFQKSLDQIFETLENKNSSSVEEL
Human *HEPP*	121	HTQGPVSDLCPVTSAQAPRHLQSSAWEMDGPRENRGSFHKSLDQIFETLETKNPSCMEEL
Mouse *Hepp*	177	FSDVDSSYYDLDTVLTGMMSGIKSSLQNGLEGFAAAATPPPSSTCKSDLAELDHVVEILVE
Human *HEPP*	181	FSDVDSPYYDLDTVLTGMMGGARPGPCEGLEGLAPATPGPSSSCKSDLGELDHVVEILVE
Mouse *Hepp*	237	T
Human *HEPP*	241	T

FIG. 3

```
Zebrafish Hepp   1  MFSKGIKRKFADGGEEISDDGLVAARVASSYSLQRQSLLDMSLIKLQLCHMLVEPNLCRS
Mouse Hepp       1  MFARGLKRKYG----DQEEGVEGFGTVPSYSLQRQSLLDMSLVKLQLCHMLVEPNLCRS
Human HEPP       1  MFARGLKRKCVGH-EEDVEGALAGLKIVSSYSLQRQSLLDMSLVKLQLCHMLVEPNLCRS

Zebrafish Hepp  61  VLIANTVRQIQEEMTHDGSWHMVTEAFCGASQSPSERLVATEVLCR------------
Mouse Hepp      56  VLIANTVRQIQEEMSQDGVWHGMAPQNVDR--APMERLVSTEILCRTVRGAEEEHPAPEL
Human HEPP      60  VLIANTVRQIQEEMTQDGTWRTVAPQAAER--APLDRLVSTEILCRAAWGQEGAHPAPGL
```

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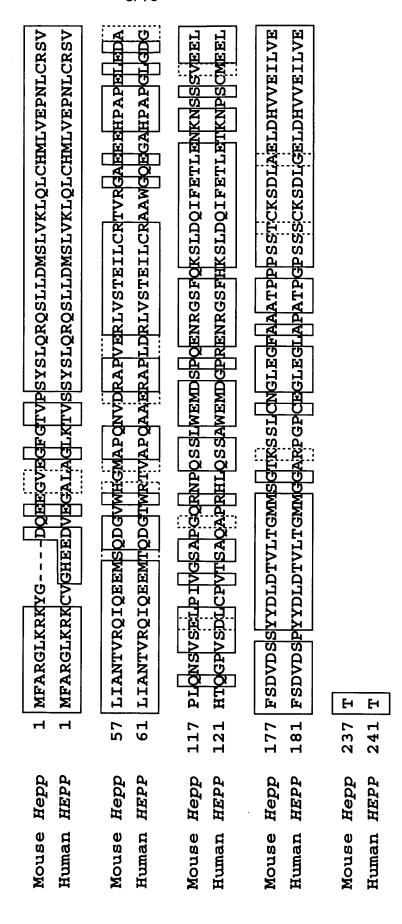Docket No. 39532-176599
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FIG. 4B

FIG. 4A

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FIG. 5

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FIG. 6B

MWM
LyD9 (lymphoid progenitor)
NFS 70 (pro-B lymphoma)
1881 (pro-B cells)
Ba/F3 (pre-B cells)
70Z/3 (pre-B cells)
NFS 5 (pre-B lymphoma)
CH33 (B cells)
M12 (B cells)
A20 (B cell lymphoma)
J558 (B cell lymphoma)
WEHI 279 (B cell lymphoma)

FIG. 6A

MWM
Thymus
WEHI 7.1 (T cell lymphoma)
EL4 (T cell lymphoma)
Spleen
FDC-P1 (myeloid progenitor)
J774 (monocyte-macrophage)
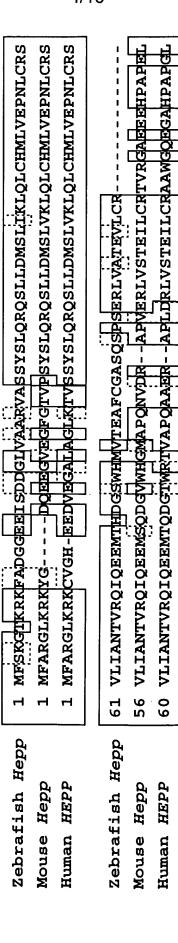RAW309 (monocyte-macrophage)
Neg. control
MWM

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FIG. 7

Chromosome 14

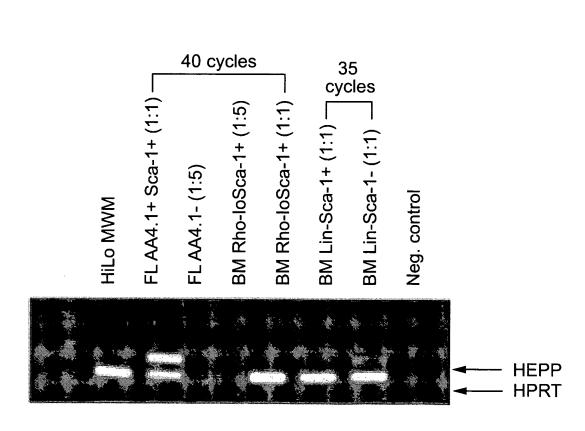|	
14p12	13
14p11.2	12
p	
14cen	11.2
	11.1
	11.1
	11.2
14q13	12
14q21	13.2 — 13.1
	13.3
	21.1
	21.2 —
	21.3
	22.1
q	22.2 — 22.3
14q24.1	23.1
	23.2 — 23.3
14q24.3	24.1
	24.2
14q32.1	24.3
	31.1
	31.2 —
14q32	31.3
	32.11 — 32.12
14q32.3	32.13 — 32.2
	32.31 — 32.32
	32.33

translocation breakpoints

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FIG. 8

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FIG. 9

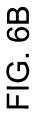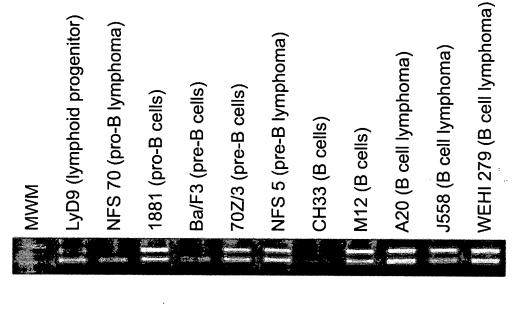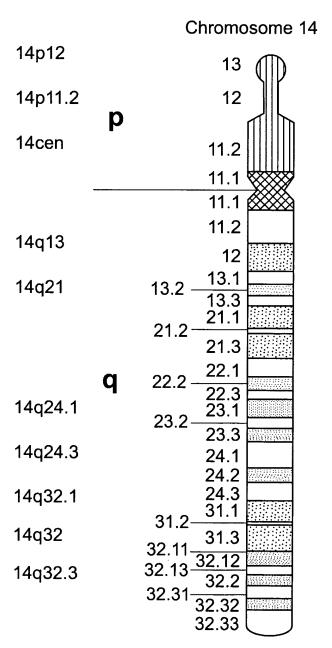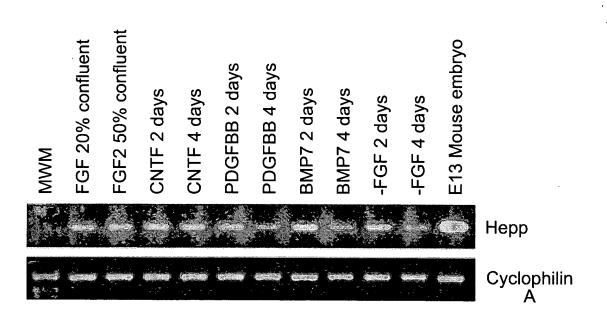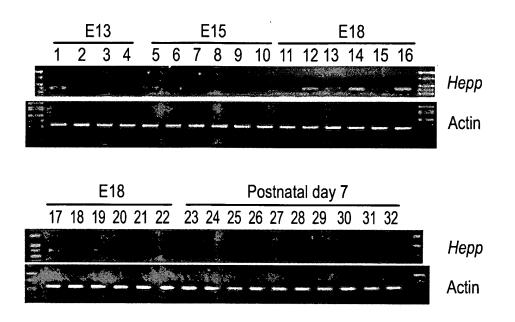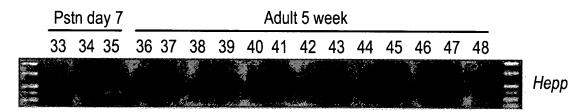| Embryo day 13	Embryo day 18	Postnatal day 7	Adult 5 week
1. Teleocephalon/Diencephalon	11. Frontal cortex	23. Frontal cortex	36. Frontal cortex
2. Mescocephalon (Midbrain)	12. Posterior cortex	24. Posterior cortex	37. Posterior cortex
3. Rhombeocephalon (Hindbrain)	13. Entorhinal cortex	25. Entorchinal cortex	38. Entorhinal cortex
4. Spinal cord	14. Olfactory bulb	26. Olfactory bulb	39. Olfactory bulb
	15. Hippocampus	27. Hippocampus	40. Hippocampus
	16. Striatum	28. Striatum	41. Striatum
	17. Thalamus	29. Thalamus	42. Thalamus
Embryo day 15	18. Hypothalamus	30. Hypothalamus	43. Hypothalamus
5. Teleocephalon	19. Midbrain	31. Cerebellum	44. Cerebellum
6. Diencephalon	20. Pons	32. Midbrain	45. Midbrain
7. Midbrain	21. Medulla	33. Pons	46. Pons
8. Pons	22. Spinal cord	34. Medulla	47. Medulla
9. Medulla		35. Spinal cord	48. Spinal cord
10. Spinal cord			

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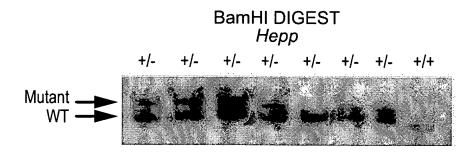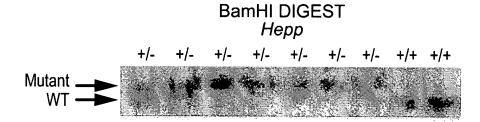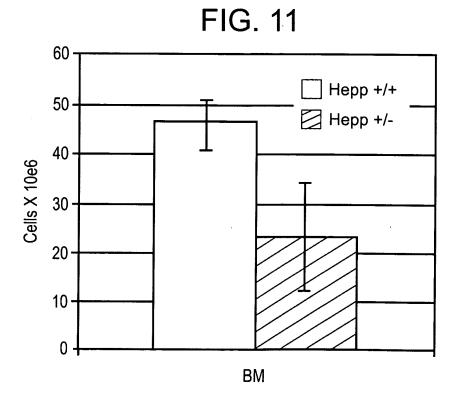Docket No. 39532-176599

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FIG. 10A

BamHI DIGEST
Hepp

FIG. 10B

BamHI DIGEST
Hepp

FIG. 11

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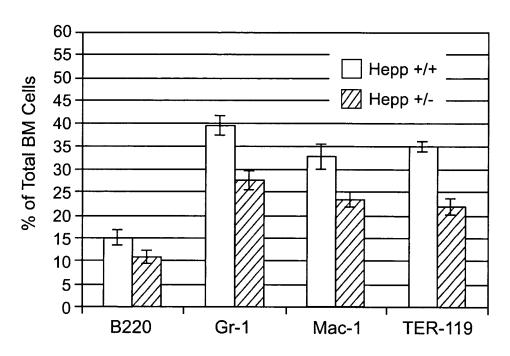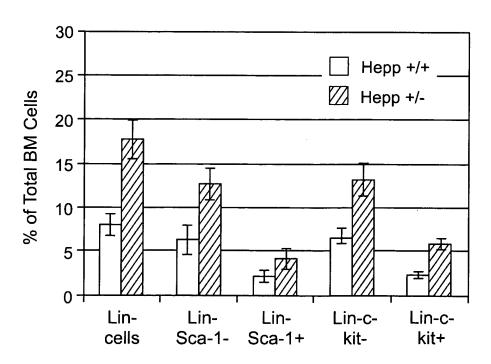Hematopoietic and Neural Development"
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FIG. 12

FIG. 13

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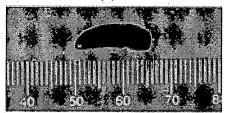Hematopoietic and Neural Development"
Docket No. 39532-176599
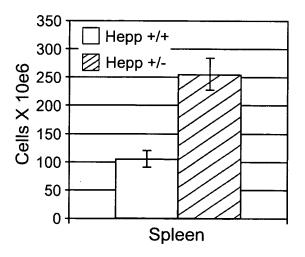
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FIG. 14

FIG. 15A

Hepp +/+

FIG. 15B

Hepp +/-
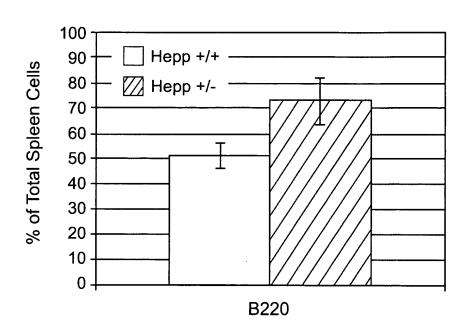

FIG. 15C

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FIG. 16A

FIG. 16B

FIG. 16C

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FIG. 17A

FIG. 17B

SPLEEN

16.9%

FIG. 17C

SPLEEN

13.1%

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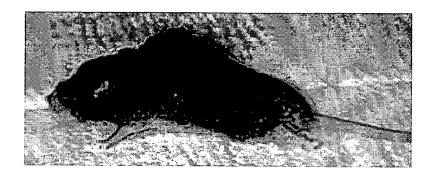Hematopoietic and Neural Development"
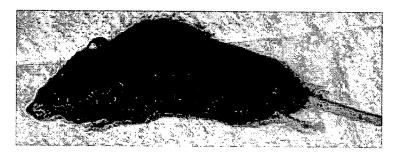Docket No. 39532-176599
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FIG. 18A

FIG. 18B

FIG. 18C